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## NOTICE OF ALLOWANCE AND ISSUE FEE DUE

15M1/0327

GERALD F SWISS  
BURNS DOANE SWECKER AND MATHIS  
P O BOX 1404  
ALEXANDRIA VA 22313-1404

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
08/507,863	07/27/95	015	NILAND, P	1511 03/27/97
First Named Applicant	GREFF, RICHARD J.			

TITLE OF INVENTION NOVEL COMPOSITIONS FOR USE IN EMBOLIZING BLOOD VESSELS

ATTY'S DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEES DUE	DATE DUE
1 018413-002	424-009.411	L16	UTILITY	YES	\$645.00	06/27/97

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT.  
PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

### HOW TO RESPOND TO THIS NOTICE:

- I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as yes, verify your current SMALL ENTITY status:

A. If the status is changed, pay twice the amount of the FEE DUE shown and notify the Patent and Trademark Office of the change in status, or

B. If the status is the same, pay the FEE DUE shown above.

If the SMALL ENTITY is shown as NO:

A. Pay FEE DUE shown above, or

B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.

- II. Part B of this notice should be completed and returned to the Patent and Trademark Office (PTO) with your ISSUE FEE. Even if the ISSUE FEE has already been paid by charge to deposit account, Part B should be completed and returned. If you are charging the ISSUE FEE to your deposit account, section "6b" of Part B should be completed.

- III. All communications regarding this application must give application number and batch number.

Please direct all communication prior to issuance to Box ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**



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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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08/507,863 07/27/95 GREFF

R 018413-002

EXAMINER

15M1/0327

GERALD F SWISS  
BURNS DOANE SWECKER AND MATHIS  
P O BOX 1404  
ALEXANDRIA VA 22313-1404

NILAND P

ART UNIT PAPER NUMBER

1511  
DATE MAILED:

03/27/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### NOTICE OF ALLOWABILITY

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

- This communication is responsive to the letter of 3/19/97.
- The allowed claim(s) is/are 1-15.
- The drawings filed on \_\_\_\_\_ are acceptable.
- Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All  Some\*  None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
- Applicant MUST submit NEW FORMAL DRAWINGS
- because the originally filed drawings were declared by applicant to be informal.
- including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. \_\_\_\_\_.
- including changes required by the proposed drawing correction filed on \_\_\_\_\_, which has been approved by the examiner.
- including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

#### Attachment(s)

- Notice of References Cited, PTO-892
- Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- Notice of Draftsperson's Patent Drawing Review, PTO-948
- Notice of Informal Patent Application, PTO-152
- Interview Summary, PTO-413
- Examiner's Amendment/Comment
- Examiner's Comment Regarding Requirement for Deposit of Biological Material
- Examiner's Statement of Reasons for Allowance

*Patrick Niland*  
PATRICK NILAND  
PATENT EXAMINER  
ART UNIT 1511

Art Unit: 1511

1. The following is an examiner's statement of reasons for allowance:

The instant claims require specific amounts of specific, water insoluble contrast agents in the composition claims and in the method of using the composition, which the cited prior art does not disclose. The instantly claimed contrast agents are known as biocompatible contrast agents but are not disclosed as useful in the instantly claimed embolizing compositions nor in the instantly claimed amounts in the instantly claimed embolizing compositions. The primary reference cited in the previous office actions (Tanabe et al.) discloses the use of "X-ray contrast medium" generically at column 11, lines 50-53. Tanabe et al. gives no further guidance in the choice of X-ray contrast medium" nor amount thereof and does not disclose the instantly claimed contrast agents, amounts thereof, nor address the affects of various types of contrasting agents. The only analogous art, as defined by In re Wood and Eversole, 202 USPQ 171, seen by the examiner is that of Taki et al., "A New Liquid Material for Embolization of Arteriovenous Malformations", which discloses the use of water soluble metrizamide as their contrast agent. See the instant application, example 3 of page 16 and the applicant has supplied Taki et al., "A New Liquid Material for Embolization of Arteriovenous Malformations". The examiner has stated, in the past office actions, that the use of water insoluble pigments in polymer solutions, i.e. paint, is well known and that such pigments do not dissolve from the film resulting therefrom. Such consideration falls within the scope of the prior art outside the instant inventors field of endeavor but the prior art which is reasonably pertinent to the particular problem with which the inventor was involved, as referred to by In re Wood and Eversole, 202 USPQ 171. The examiner also

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notes that water soluble dyes are also used in polymers and such dyes are not disclosed as materially affecting the properties of the dyed polymer. It is also noted that these examples considered by the examiner are not disclosed for the unique application as embolizing compositions either. The applicant has argued that, at best, the ordinary skilled artisan would have been led to believe that the instantly claimed contrasting agents were "equivalents" of the metrizamide of the analogous prior art. The examiner believes that it is clear that soluble dyes and insoluble pigments are not exactly "equivalent". Obviously, they differ in solubility and other properties known to the ordinary skilled artisan. However, these compounds are "equivalent" in that their purpose is to add "color" to the pigmented or dyed polymer without materially affecting the physical properties of the polymer in a negative manner. In this case, "color" is used broadly to include the instantly required X-ray opaqueness. For instance, it is known that solid particles of pigment bonded to polymer matrix increase the modulus, but the amount of pigment is chosen so that the polymer matrix does not disintegrate. It is equally true that soluble dyes are chosen so that the polymer matrix does not disintegrate. The instantly claimed composition does not bond, the contrasting agent to the polymer. The examiner observed this first hand in the demonstration of the interview of 10/17/96 and Taki et al., "A New Liquid Material for Embolization of Arteriovenous Malformations" discloses the EVAL as being non-adhesive. This is critical to the examiner's decision to allow the instant claims because the fact that the insoluble contrasting agent does not adhere to the polymer of the instant claims might have been expected to produce a product of inferior physical properties to the metrizamide composition of Taki et al.. The

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examiner notes the common practice of using "coupling agents" in the filled polymer art to increase polymer/filler bonding so as to increase the physical properties thereof. The examiner notes the applicant's showing that metrizamide increases the viscosity of the EVAL solution. It is clear that such increased viscosity will produce undesirable pressures of injection where the viscous material is injected into an already weak arteriovenous malformation. It is not the subject of this reason for allowance to determine whether this viscosity increase of metrizamide verses the instantly claimed contrasting agents is unexpected. The examiner does not have enough information for this. However, the increase of viscosity indicates that the metrizamide forms some sort of secondary bonding with the EVAL which might have been expected to give the adequate interaction of metrizamide with the EVAL to make it an acceptable "dye-type" contrasting agent. Indeed, it is the only contrasting agent specifically disclosed for use in the ethylene vinyl alcohol/DMSO embolizing compositions. Note that page 166 of Taki et al., "A New Liquid Material for Embolization of Arteriovenous Malformations" discloses the presence of "EVAL fragments". This is consistent with the applicant's declaration of 3/19/97, which describes the metrizamide containing embolizing compositions as being "a loosely defined precipitate...having the consistency of tissue/toilet paper when exposed to water". The instantly claimed compositions form a well defined solid mass when precipitated in water, according to the applicant's declaration and the results observed by the examiner at the interview of 10/17/96. The examiner and the applicant agreed that the instantly claimed showings were what was expected to give the precipitate that was most affected by water due to its large content of hydrophilic vinyl

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alcohol segments and which was most expected to fall apart based on the large ratio of binding EVOH copolymer to contrasting agent (note that too much particulate filler to binder will be very weak due to the lack of enough binder to hold the filler together). Given the lack of teaching in the cited prior art, it is the examiner's position that the examples of the applicant's declaration of 3/19/97 are commensurate in scope with the cited prior art and the instant claims. It is the examiner's position that the difference in physical nature and properties of the precipitated product of the instant claims over the precipitated product of the cited analogous art is unexpected based upon the teachings of the cited prior art and the other considerations made by the examiner. For these reasons, the instant claims are allowable over the cited prior art. The method of claims 7-15 is allowable for the same reasons as the composition claims.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Niland whose telephone number is (703) 308-3510.

pn

March 26, 1997



Patrick Niland  
Patent Examiner  
Art Unit 1511